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Clinicopathologic Study of Advanced Gastric Cancer Without Serosal Invasion in Young and Old Patients

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Fifty-seven patients treated by radical gastric resections were retrospectively studied to understand the clinicopathologic characteristics of advanced gastric cancer without serosal invasion (the depth of tumor invasion limited to the muscularis propria or subserosal layer) in young and old age persons. There were 36 patients in the old age group (age >60 years) and 21 in the young age group (age ≦40 years). The clinical and pathologic parameters for this study included sex, gross type, location, maximum tumor size, depth of invasion, lymph node metastasis, tumor stage, histologic type, and rate of curative resection. The old patients had a higher percentage of small tumors, subserosal invasion and lymph node metastasis, but these parameters were not significantly different from those of the young patients, nor did the sex ratio, gross type, location, and rate of curative resection show significant differences. The histologic feature was the only statistically significant parameter, determined by univariate and multivariate analyses. Poorly differentiated adenocarcinoma and signet ring cell carcinoma were detected in 10 (47.6%) and 4 (19.0%) of the 21 younger patients, respectively, while there were 4 (11.1%) and 2 (5.6%) in the old age group. Although the gastric cancer in young patients had more aggressive histologic characteristics than it did in elderly patients, survival rates between the two groups did not differ to any great degree. Our findings indicate that the prognosis for younger patients with advanced gastric cancer without serosal invasion was favorable when curative resection was performed.

KEY WORDS: gastric cancer in young patients, advanced gastric cancer without serosal invasion

INTRODUCTION

Although the incidence of gastric cancer has generally decreased worldwide [1–5], the disease is still one of the most frequent malignancies in Taiwan. Gastric cancer is the third major cause of cancer-related death among males and the fifth major cause of cancer-related death among females [6]. Although its mortality rate has declined gradually during recent years, approximately 2,000 people died of gastric cancer in 1991 in Taiwan [6]. Most cases occurred in elderly individuals, with the peak incidence in patients over 60 years of age [3,6,7]. The incidence of gastric cancer for patients aged 40 years and younger ranged from 2.4% to 7.9% [7–9]. Although delay in diagnosis and rapid progress of disease in younger patients are frequently cited as the main reasons for the poor prognosis in young adults [8,10,11], the precise nature of the relationship between the prognosis and age of

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TABLE I. Comparison of Clinicopathologic Factors Between Young Adults and the Elderly in Advanced Gastric Cancer Without Serosal Invasion

	Age ≦ 40 yr (n = 21)	Age > 60 yr (n = 36)	*P*
Male/female	9/12	22/14	0.18197
Age (yr)	34.9 ± 1.1[a]	67.1 ± 0.8[a]	
Depth of invasion			
mp	13	15	0.14040
SS	8	21	
Gross type			
Borrmann I	1	2	
Borrmann II	6	13	
Borrmann III	12	19	0.73232
Borrmann IV	2	1	
Borrmann V	0	1	
Location			
Upper third	1	4	
Middle third	7	7	0.41390
Lower third	13	25	
Maximum tumor diameter			
<5 cm	13	23	0.88092
≧5 cm	8	13	
Lymph node metastasis			
Positive	12	25	0.34787
Negative	9	11	
Stage (JRSGC)[b]			
I	9	11	
II	5	9	0.71828
III	6	15	
IV	1	1	
Histologic features			
Well-differentiated	4	10	
Moderately differentiated	2	15	
Poorly differentiated	10	4	0.00369
Signet ring cell	4	2	
Mucinous	1	5	
Curability of resection			
Curative	19	33	1.00000
Noncurative	2	3	

[a] Mean ± SE.
[b] Japanese Research Society for Gastric Cancer.

patients with gastric cancer remains a controversial issue. According to the criteria proposed by the Japanese Research Society for Gastric Cancer [12], advanced gastric cancer is divided histologically by depth of invasion into four subgroups: muscularis propria (mp), subserosa (ss), serosa-exposed (se), and serosa-infiltrating (si). Those patients with advanced gastric cancer without serosal invasion (including mp and ss cancers) have a more favorable prognosis than those with serosal invasion (including se and si cancers) [13]. Although young and old patients with gastric cancer have been the subject of reports [7–11], it remains unknown as to whether advanced gastric cancer without serosal invasion in young adults has different clinicopathologic characteristics from that in older adults. The purpose of the present study is to identify the clinicopathologic characteristics of disease and survival rates in young and old patients with advanced gastric cancer without serosal invasion.

MATERIALS AND METHODS

Patients

From January 1981 to December 1992, 426 patients with gastric carcinoma were admitted to the Department of Surgery of Kaohsiung Medical College Hospital. Of these, 57 patients with advanced gastric cancer without serosal invasion underwent radical gastric resection. Of these patients, 21 were 40 years of age or younger (young age group), and 36 were more than 60 years of age (old age group). The young age group consisted of 9 males and 12 females, while the old age group consisted of 22

males and 14 females. Chemotherapy with 20 mg of intravenous mitomycin was given immediately after surgical resection to each patient, and another 10 mg was given on the following day. These patients formed the subjects of this study. All patients had a primary adenocarcinoma of the stomach and had no evidence of any other malignancy. The results of the surgery were carefully followed up until December 1994. The clinicopathologic records of these patients included sex ratio, depth of invasion, gross type, location, maximum tumor size, lymph node metastasis, microscopic stage, histologic features, curability of resection, and survival rates. Clinicopathologic descriptions were carried out according to the General Rules for the Gastric Cancer Study in Surgery and Pathology from the Japanese Research Society for Gastric Cancer [12]; all tissues were examined by pathologists. When two histologic types coexisted in the tissue, the pathologic diagnosis was based on the predominant histologic type.

Statistical Analysis

All data analyses were made using the SPSS for Windows statistical software package (SPSS, Chicago, IL). The long term survival rate was estimated using the Kaplan–Meier method, and the log-rank test was used to quantify statistical differences. The chi-square test with Yates's correction and the Fisher exact test were used for analysis of other parameters analysis. In addition, multivariate adjustment was performed by the logistic regression analysis. The level of statistical significance was $P < 0.05$.

RESULTS

Clinicopathologic Findings

Table I shows the clinicopathologic features of advanced gastric cancer without serosal invasion according to age group. The mean age of patients in the young age group was 34.9 ± 1.1 years and that of the old age goup was 67.1 ± 0.8 years. Of 21 young patients and 36 old patients, the male to female ratios were 4:5 and 8:5, respectively. The proportion of female patients in the young age group is higher than the old age group ($P = 0.18197$). With regard to the depth of tumor invasion, no significant differences existed between the two groups ($P = 0.14040$). In terms of gross type in the primary lesion, Borrmann III was the most common type in both groups. In this, there was no statistical difference between the two groups ($P = 0.73232$). With respect to primary tumor location in the stomach, most tumors were located in the lower third portion of the stomach (61.9% in the young age group and 69.4% in the old age group) ($P = 0.4139$). As for maximum tumor size, lesions larger than 5 cm were found in 61.9% and 63.9%, respectively, for patients in the young group and old group ($P = 0.88082$).

TABLE II. Advanced Gastric Cancer: Logistic Regression Analysis for Variables Associated With Age (≤40 or >60 Years)

Variables (observed value)	*P*	Adjusted odds ratio
Sex ratio (male, female)	0.0830	1.85
Depth of invasion (mp, ss)	0.2093	0.63
Lymph node metastasis (positive, negative)	0.2095	1.61
Histologic features (well + moderately differentiated, poorly differentiated + signet ring cell + mucinous)	0.0008	3.59

mp, muscularis propria; ss, subserosa.

No statistically significant differences were found regarding lymph node metastasis ($P = 0.34787$), stage ($P = 0.71828$) and curability of resection ($P = 1.0000$). However, a significant difference was found in the histologic features ($P = 0.00369$). With regard to the histologic features of the primary tumor, there were 10 (47.6%) patients with poorly differentiated adenocarcinoma and 4 (19.0%) patients with signet ring cell carcinoma in the young age group; these rates of incidence were markedly higher than those in the old age group. Poorly differentiated adenocarcinoma and signet ring cell carcinoma was observed in 11.1% and 5.6% of old patients, respectively. The incidence of well-differentiated adenocarcinoma plus moderately differentiated adenocarcinoma was 28.6% in young patients, and 69.4% in elderly patients.

Multivariate Analysis

The results of multivariate analysis using the covariates of sex ratio, depth of invasion, lymph node metastasis and histologic features by the logistic regression analysis method is shown in Table II. Among the covariates, only histologic features of the primary lesion showed a significant difference between the two groups.

Survival Rates

Figure 1 shows the postoperative survival curves of the young and old age groups. The 5-year survival rate was 58.3% for patients in the young age group and 55.5% for patients in the old age group. The survival rate for patients in the two groups did not differ significantly ($P = 0.8427$).

DISCUSSION

Gastric carcinoma occurs most commonly in patients over 60 years of age [6–8] and only infrequently in patients aged 40 years or younger. The relations between the clinicopathologic patterns and survival rate of gastric carcinoma in young adults and those in old patients have been studied by previous investigators [7–11]. They suggested that there is a higher proportion of female patients and of poorly differentiated adenocarcinoma in young

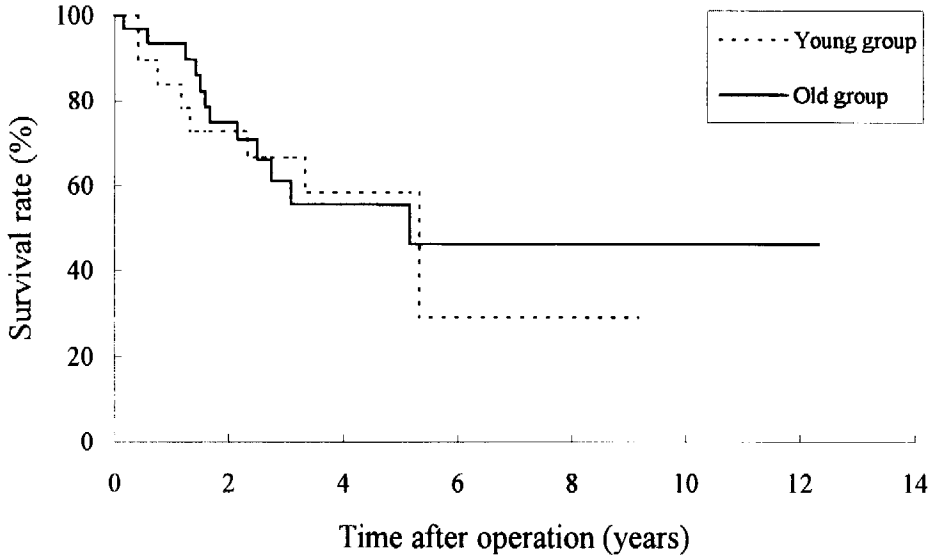

Fig. 1. Survival rates for advanced gastric cancer without serosal invasion in both young (≦40 years) and old age groups (>60 years). There was no significant difference between the two gorups (P >0.05).

patients. It has been a controversial issue that the survival rate of young patients differed from that of old patients. Some investigators pointed out that if the lesion did not invade beyond the muscularis propria layer, the prognosis for young patients was not worse than that for the general population for gastric cancer [9,14,15].

Whether the clinicopathologic features and survival rates in younger patients with advanced gastic cancer without serosal invasion are different from those in older patients is an interesting topic. Our retrospective study revealed that the histologic feature was the only statistically significant factor found by univariate and multivariate analyses; though there was a greater percentage of female patients in the young group, compared with findings in the old age group. Of the patients in our study, the male to female ratio was around 4:5 in young patients and it increased up to 8:5 in old patients. The female preponderance among the younger patients in the present series is in agreement with the literature and contrasts with the consistent preponderance of men that is typically found in the elderly [7–11]. This reversal in sex ratio may be related to the effect of the sex hormones on cancer development [16].

We found marked differences between the young and old age groups when we compared the histologic features. The higher incidence of poorly differentiated type of gastric cancer (including poorly differentiated adenocarcinoma and signet ring cell carcinoma) in young patients is consistent with the literature [7,9], and this may be due to lack of cancer cell differentiation in the young. A greater percentage of the diffuse type by Lauren system [17] or infiltrative type by Ming system [18] was also noted in the young adults [8,19]. Although the young age group presented more aggressive histologic characteristics than the old age group, any differences in survival rates between the two groups were not statistically significant. It may be suggested that the histologic feature was not an independent prognostic factor influencing the outcome of either group. Bedikian et al. [14] and Bloss et al. [11] reported that young gastric cancer patients having poor prognoses was due to delays in the diagnosis rather than to the pathological characteristics of gastric cancer. Perhaps because our study was restricted to mp and ss gastric cancers, the prognosis for the young patients was not as unfavorable as previously reported. The rates of curative operations were as high as 90.4% in the young patients and 91.6% in the elderly patients in our series. At the same time, the 5-year survival rates in the two age groups were not significantly different. The study thus indicates that age alone should not be a reason for withholding surgical treatment from younger patients with advanced gastric cancer without serosal invasion. We propose that a radical procedure should be applied to both younger and older patients with advanced gastric cancer, especially if the lesion had been detected before the cancer reached the serosal layer.

CONCLUSION

The data on 57 patients with advanced gastric cancer without serosal invasion were analyzed with respect to clinicopathologic features and survival rates according to age. When we compared the young patients with the elderly patients, we found the only difference was the histologic pattern. Fourteen (66.7%) of the young group had a poorly differentiated adenocarcinoma or signet ring cell carcinoma, whereas only 6 (16.7%) were found in the old age group. Despite the more aggressive histologic characteristics of the disease in young age group than in

the old age group, the prognosis for young patients with advanced gastric cancer without serosal invasion is not unfavorable when curative resection is performed.

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